

Attorney Docket No. FM-10-US

Serial No.: 10/517,904

AMENDMENTS TO THE SPECIFICATION

In paragraph [0001] of the specification, please amend paragraph [0001] as follows:

[0001] This application is a U.S. filing under 35 U.S.C. 371 of PCT/EP03/06193, filed on June 12, 2003, which claims the benefit of GB 0213614.1 filed on June 13, 2002, the disclosures of each of which are incorporated herein by reference. The current invention relates to a kinase active in the protein kinase B (PKB) signaling pathway and to the use of the kinase, and to methods of identifying modulators thereof. More particularly, the present [11] invention relates to a purified kinase that phosphorylates the Ser 473 residue of PKB in vivo, and to a method of identifying molecules that regulate signal transduction through the kinase.

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AMENDMENTS TO THE CLAIMS

Please amend the claims as follows.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

~~Claim 1: (Cancel) A cell-free composition comprising a complex which has PKB Ser 473 kinase activity and an apparent molecular weight of 450-650 kDa.~~

~~Claim 2: (Cancelled)~~

~~Claim 3: (Cancel) The cell-free composition of claim 1, wherein said complex comprises a protein having a molecular weight of 48 kDa as estimated by SDS gel electrophoresis.~~

~~Claim 4: (Cancel) The cell-free composition of claim 1, wherein said complex comprises a protein having a molecular weight of 58 kDa as estimated by SDS gel electrophoresis.~~

Claim 1.

~~Claim 5: (Currently amended) A purified PKB Ser 473 kinase protein complex, which has PKB Ser 473 kinase activity and an apparent molecular weight of 450-650 kDa when fractionated by gel filtration chromatography, wherein the purified PKB Ser 473 kinase complex has been isolated from a cell-free extract that has measurable PKB Ser 473 kinase activity in 0.2 μ g of protein when detected in a kinase assay in which a PKB peptide substrate is phosphorylated with 32 P labeled phosphate, wherein the purified PKB Ser 473 kinase complex elutes with the apparent molecular weight of 450-650 kDa when fractionated by the gel filtration chromatography and the measurable PKB Ser 473 kinase activity in the cell-free extract is at least 2000 times greater than a PKB Ser 473 kinase activity in a crude cell extract, wherein the kinase activities are measured using the kinase assay.~~

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~~Claim 6. (Cancelled)~~

Claim 2.

~~Claim 7.~~ (Currently amended) A purified cell extract that has measurable PKB Ser 473 kinase activity in 0.2 µg of protein when detected in a kinase assay in which a PKB peptide substrate is phosphorylated with ³²P label[[I]]ed phosphate, wherein [[the]] a kinase complex elutes with an apparent molecular weight of 450-650 kDa when fractionated by gel filtration chromatography and the measurable ~~PKB Ser 473 kinase~~ activity in the purified cell extract is at least 2000 times greater than ~~a specific activity of a PKB Ser 473 kinase activity in a crude cell extract wherein the kinase activities are measured using the kinase assay.~~

Claim 3.

~~Claim 8.~~ (Currently amended) The purified cell extract of claim 7, wherein the kinase complex elutes with an apparent molecular weight of 550 kDa when fractionated by gel filtration chromatography.

~~Claim 9. (Cancelled)~~

~~Claim 10. (Withdrawn) A method for producing antibodies which selectively bind to a purified~~
~~PKB Ser 473 kinase protein comprising the steps of:~~
~~i) administering an immunogenically effective amount of a PKB Ser 473 kinase~~
~~immunogen to an animal;~~
~~ii) allowing the animal to produce antibodies to the immunogen; and~~
~~iii) obtaining the antibodies from the animal or from a cell culture derived therefrom.~~

~~Claim 11. (Withdrawn) A PKB Ser 473 kinase specific antibody.~~

Claim 4.

~~Claim 12.~~ (Withdrawn and currently amended) A method of screening for a ~~potential~~ modulator of PKB Ser 473 kinase activity comprising the steps of:

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(i) incubating the purified PKB Ser 473 kinase ~~protein~~ complex of claim ~~[[s]]~~ 5 ~~or~~ 6 with a compound;

(ii) determining PKB Ser 473 kinase activity; and

(iii) detecting an alteration in the PKB Ser 473 kinase activity in the presence of the compound relative to when ~~[[said]]~~ the compound is absent, ~~[[said]]~~ the alteration being indicative of a ~~potential~~ modulator of PKB Ser 473 kinase activity.

Claim 5.

~~Claim 13:~~ (Withdrawn and currently amended) The method according to claim 12, wherein ~~[[said]]~~ the alteration in the PKB Ser 473 kinase activity is a decrease in PKB Ser 473 kinase activity, ~~[[said]]~~ the decrease being indicative of an ~~potential~~ inhibitor of PKB Ser 473 kinase.

Claim 6.

~~Claim 14:~~ (Withdrawn and currently amended) The method ~~as claimed in~~ according to claim 12, wherein ~~[[said]]~~ the alteration in the PKB Ser 473 kinase activity is an increase in the PKB Ser 473 kinase activity, ~~[[said]]~~ the increase being indicative of an ~~potential~~ activator of PKB Ser 473 kinase.

~~Claim 15:~~ (Withdrawn) A modulator of PKB Ser 473 kinase activity.

~~Claim 16:~~ (Withdrawn) The modulator of claim 15 for use as a pharmaceutical.

~~Claim 17:~~ (Withdrawn) The use of the modulator of claim 15 for the manufacture of a ~~medicament for the treatment or prophylactic treatment of a condition associated with~~ cell growth.

~~Claim 18:~~ (Withdrawn) The use as claimed in claim 17, wherein said condition is tumour cell growth.

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~~Claim 19. (Withdrawn) The use of the modulator of claim 15 for the manufacture of a~~
~~medicament for the treatment or prophylactic treatment of diabetes, neurodegenerative~~
~~conditions or erectile dysfunction, wherein said modulator is an activator.~~

~~Claim 20. (Withdrawn) A method for inhibiting cancer cell growth comprising contacting a~~
~~cancerous cell with a PKB-Ser 473 kinase inhibitor.~~

~~Claim 21. (Withdrawn) A method for treating a disease associated with an anomaly in cell~~
~~growth comprising administering to a subject a pharmaceutically effective amount of a~~
~~PKB-Ser 473 kinase inhibitor.~~

~~Claim 22. (Withdrawn) A method for treating a disease associated with an anomaly in cell~~
~~growth comprising administering to a subject a pharmaceutically effective amount of a~~
~~PKB-Ser 473 kinase inhibitor.~~

~~Claim 23. (Withdrawn) A method for treating a disease associated with an anomaly in insulin~~
~~regulation, neurodegeneration or erectile dysfunction comprising administering to a~~
~~subject a pharmaceutically effective amount of a PKB-Ser 473 kinase activator.~~